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L3: Entry 4 of 61 File: USPT Jul 2, 2002

DOCUMENT-IDENTIFIER: US 6413539 B1
TITLE: Hydrogel-forming, self-solvating absorbable polyester copolymers, and methods for use thereof

Brief Summary Text (11):
U.S. Pat. No. 3,991,766, to Schmitt et al., discloses absorbable articles made of polyglycolide, such as sutures, clips and storage pallets having medicaments incorporated therein and can be used for both their own mechanical properties and delayed release systems of medicaments. U.S. Pat. No. 5,171,148, to Wasserman et al., discloses the use of absorbable polymers made from p-dioxanone or L-lactide and glycolide as dental inserts for the treatment of periodontal disease. Here, a semiporous mesh material with sealed edges is emplaced between the tooth and gingiva. The implant is attached to the tooth by an absorbable ligature material. U.S. Pat. No. 5,198,220, to Damani, discloses the treatment of periodontal disease through the use of a sustained release composition/device comprising bioactive agents. The composition/device is in a liquid, semi-solid or solid form suitable for insertion into or around the periodontal pocket. Damani also teaches the formation of a gel, or paste, composition consisting of poly(lactyl-co-glycolide) in an acceptable solvent (such as propylene carbonate), with or without propylene and/or polyethylene glycol, and an antibiotic agent such as tetracycline hydrochloride.

Brief Summary Text (12):
Other in-situ forming biodegradable implants and methods of forming them are described in U.S. Pat. Nos. 5,278,201 ('201 Patent) and 5,077,049 ('049 Patent), to Dunn et al. The Dunn et al., patents disclose methods for assisting the restoration of periodontal tissue in a periodontal pocket and for retarding migration of epithelial cells along the root surface of a booth. The '049 Patent discloses methods which involve placement of an in-situ forming biodegradable barrier adjacent to the surface of the tooth. The barrier is microporous and includes pores of defined size and can include biologically active agents. The barrier formation is achieved by placing a liquid solution of a biodegradable polymer, such as poly(dl-lactide-co-glycolide) water-coagulatable, thermoplastic in a water miscible, non-toxic organic solvent such as N-methyl pyrrolidone (i.e., to achieve a typical polymer concentration of .ltoreq.50%) into the periodontal pocket. The organic solvent dissipates into the periodontal fluids and the biodegradable, water coagulatable polymer forms an in-situ solid biodegradable implant. The dissipation of solvent creates pores within the solid biodegradable implant to promote cell ingrowth. The '859 Patent likewise discloses methods for the same indications involving the formation of the biodegradable barrier from a liquid mixture of a biodegradable, curable thermosetting prepolymer, curing agent and water-soluble material such as salt, sugar, and water-soluble polymer. The curable thermosetting prepolymer is described as an acrylic-ester terminated absorbable polymer.

Brief Summary Text (18):
U.S. Pat. No. 5,366,756, to Chesterfield et al., describes a method for preparing porous bioabsorbable surgical implant materials. The method comprises providing a quantity of particles of bioabsorbable implant material, and coating particles of bioabsorbable implant material with at least one growth factor. The implant can also contain antimicrobial agents.

Brief Summary Text (21):
To date, the known HHDS and thermoreversible gels can be classified as non-absorbable materials and are expected not to absorb through chain dissociation in the biological environment. Meanwhile, there is a growing interest in developing absorbable sutures and allied surgical devices such as transient implants, which are degraded to bioabsorbable, safe by-products and leave no residual mass at the surgical site, as

well as frequently cited clinical advantages (Shalaby, Chap. 3 in High Technology Fibers (M. Lewin & J. Preston, eds.), Dekker, New York, 1985; Shalaby, 1988, cited elsewhere herein; Shalaby, Polym. News, 16, 238, 1991; Shalaby, J. Appl. Biomater., 3, 73, 1992; Shalaby, Biomedical Polymers: Designed to Degrade Systems, Hanser Publ., New York, 1994; and Shalaby, et al, eds. Polymers of Biological & Biomedical Significance, Vol. 520, ACS-Symp. Ser., Amer. Chem. Soc., Washington, 1993) have justified the need for novel absorbable hydrogel formulations.

Brief Summary Text (33):
Accordingly, the present invention provides hydrogel-forming, self-solvating, absorbable polyester copolymers capable of selective, segmental association into a compliant hydrogel mass on contact with an aqueous environment. In a preferred embodiment of the invention, the copolymer comprises a base component, designated "Component A" herein. As used herein, the terms "Component A" and "copolymer(s)" are interchangeable and refer to the basic structure of the copolymers of the invention. Component A comprises a molecular chain having a hydrophilic block, designated "Y" herein, and a relatively hydrophobic polyester block, designated "X" herein. Hydrophobic block X and hydrophilic block Y more preferably comprises a molecular structure having the following formula: X-Y-X or (X-Y).sub.n, and branched structures thereof. Most preferably, hydrophobic block X comprises a polyester formed by grafting a glycolide, lactide, .epsilon.-caprolactone, p-dioxanone, trimethylene carbonate or combinations thereof, onto the hydroxylic or amino groups of a hydrophilic polymer precursor i.e., Y; hydrophilic block Y comprises a polyoxyethylene, poly(oxyethylene-b-oxypropylene), polypeptide polyalkylene oxamate, a polysaccharide, and derivatives thereof; or a liquid, high molecular weight polyether glycol interlinked with an oxalate or succinate functionalities in linear or branched form.

Brief Summary Text (39):
The term "Hydrophobic Block(s)" as used herein, refers to absorbable polyester chain block(s) or segment(s) of variable length which, is present in an isolated form, will produce practically amorphous (with less than 5% crystallinity) or totally amorphous material having a T.sub.g of less than 25.degree. C., and preferably, is a viscous liquid at room temperature. Hydrophobic block(s) X comprises copolymeric segments of known chemistries in the art, such as, those comprised from cyclic lactones (e.g., glycolide, l-lactide, dl-lactide, .epsilon.-caprolactone, p dioxanone, trimethylene carbonate), polyalkylene oxalate, and the like, as described by Shalaby, 1988, cited elsewhere herein, which disclosure is hereby incorporated by reference. More preferably, hydrophobic segment(s) or block(s) X comprises lactide/glycolide copolymer (with 51 to 80% l- or dl-lactide).

Brief Summary Text (55):
The present invention discloses novel hydrogel-forming, self-solvating, absorbable polyester copolymers, which upon hydration results in a hydrogel mass. The hydrogel mass is stabilized by pseudo-crosslinks provided by a hydrophobic polyester component, such as those comprised from cyclic esters e.g., glycolide, l-lactide, dl-lactide, F-caprolactone, p dioxanone, trimethylene carbonate, polyalkylene oxalate, derivatives thereof and the like, covalently linked to a hydrophilic component comprised of blocks, such as those derived from a polyethylene glycol, polypeptide, polyalkylene oxamate (U.S. Pat. Nos. 4,209,607 and 4,226,243, to Shalaby et al., hereby incorporated by reference), or polysaccharide and derivatives thereof. The polyester copolymers, with or without modifying additives, undergo hydration in the biologic environment leading to selective segmental association thereby forming compliant hydrogels at the application site.

Brief Summary Text (57):
The copolymers of the invention comprise a primary or base component designated "Component A" herein. Component A comprises molecular chains having a hydrophilic block, designated "Y" herein, and a relatively hydrophobic polyester block, designated "X" herein. The molecular structure of hydrophobic block X and hydrophilic block Y preferably comprises one of the following formulas: X-Y-X or (X-Y).sub.n, and branched structures thereof. More preferably, hydrophobic block X comprises a polyester formed by grafting a glycolide, lactide, .epsilon.-caprolactone, p-dioxanone, trimethylene carbonate or combinations thereof, onto the hydroxylic or amino-end groups of a hydrophilic polymer precursor i.e., Y. Hydrophilic block Y preferably comprises a polyoxyethylene, poly(oxyethylene-b-oxypropylene), polypeptide, polyalkylene oxamate, a polysaccharide, or derivatives thereof, or a liquid, high molecular weight polyether glycol interlinked with oxalate or succinate functionalities in linear or branched form.